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LUMINESCENT CHARACTERIZATION OF INTERACTION EFFICIENCY IN THE SYSTEM "CYTISINE – AMINO ACID" AS AN INDICATOR OF ANTI-INFLAMMATORY ACTIVITY

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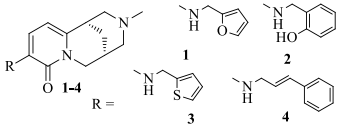
Spectral fluorescent of some 12-*N*-substituted (–)-cytisine derivatives have been studied and their relative quantum yields and lifetime in the electronically excited state have been defined. We have studied the quenching of fluorescence of *L*-tyrosine and *L*-tryptophan by amino-derivatives of 12-*N*-methylcytisine as well as the FL quenching of cytisines themselves by *L*-serine and *L*-arginine. The found Stern–Volmer constants and lifetimes of the excited states reveal static mechanism of the quenching of aromatic amino acids and dynamic mechanism for the FL quenching of cytisines by Arg (Ser does not quench FL) due to the reversible photo-induced electron transfer (PET). The thermodynamic assessment of the PET probability according to the Weller equation agrees with the observed regularities and series of bioactivity of the cytisines.



Generalization of the obtained results are presented as a rating in Table, in which the studied alkaloids **1-4** are placed according to the decrease in their activity and collated with our experimental and computational results.

This allows selecting compounds **2** and **4**, which frequently achieve two top positions in the rating table and have the highest biological activity toward COX-2 revealed with in silico screening and further verified by *in vivo* and *in vitro* tests [1].Compound **4** also takes the leading positions in the columns with the results of spectral fluorescent experiments and quantum chemical calculations. Having compared the luminescent regularities and biological activity of 3-amino-derivatives of 12-*N*-methylcytisine, we propose their interrelation. The studied alkaloids non-covalently interact with a set of amino acid residues if the enzyme active site contains such amino acids as tyrosine and tryptophan. This results in the complexation of the alkaloids with the protein molecule. On the other hand, the alkaloids facilely accept the electron from the aromatic amino acids via PET process. Thus, we assume that compounds **2** and **4** inhibit COX-2 due to the withdrawal of electron from the chain HEM–His388–Trp387–His386–Tyr385 by the interaction between **2** and **4** with tryptophan and/or tyrosine.

Table A top-down rating of biological activity of 3-amino-derivatives of 12 *N*-methylcytisine (1-4), their spectral fluorescent parameters and binding energies of ligand–protein complexation.

Biological properties [1]			Spectral fluorescent parameters				ΔG_{bind}
			Constants of FL quenching of amino acids		PET efficiency		
In silico	*In vivo*	*In vitro*	Trp	Tyr	Trp	Tyr	–
4	**4**	**2**	**4**	**4**	**4**	**4**	**4**
2	**2**	3	3	3	**2**	**2**	**2**
3	3	**4**	1	**2**	3	3	3
1	1	1	**2**	1	1	1	1

1. Tsypysheva I. et al. *AIAAMC*, 2017, in press.

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